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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/551,301

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Christopher R. Trotta

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EXAMINER

BOESEN, CHRISTIAN C

ART UNIT

PAPER NUMBER

4131

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DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/551,301	Applicant(s) TROTТА, CHRISTOPHER R.	
	Examiner CHRISTIAN BOESEN	Art Unit 4131	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 February 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 55-90 is/are pending in the application.
- 4a) Of the above claim(s) 57-62, 64, 66, 68, 70, 72, 74-77, 80 and 83-90 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 55, 56, 63, 65, 67, 69, 71, 73, 78, 79, and 81-82 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 27 September 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>01/09/2007 and 12/27/2007</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

This Non-Final Office Action is responsive to the communication received 02/17/2009. The Examiner of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Christian Boesen Art Unit 4131.

Election/Restrictions

Applicant's election with traverse of group I, claims 55-58, 63-75, and 77-82 is acknowledged. Applicant argues that it is not a burden on the examiner to search inventions of group I and group II. In response, the examiner notes that because the prior art teaches the shared technical feature of the present invention, as discussed in the art rejections below, the claims lack unity and therefore the restriction is set forth as it applies to U.S. practice. The restriction is thus deemed proper and is made FINAL.

Claims 57-62, 64, 66, 68, 70, 72, 74-77, 80, and 83-90 are withdrawn because they are drawn to the non-elected invention or species.

Claims 55-56, 63, 65, 67, 69, 71, 73, 78-79, and 81-82 are under examination in this Office Action.

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Information Disclosure Statement

The information disclosure statement (IDS) submitted on 01/09/2007 and 12/27/2007 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the Examiner.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 55-56, 65, 67, 71, and 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tocchini-Valentini (WO 01/92463; 12/6/2001; Cited in IDS of 01/09/2007), in combination with Gontarek (WO 00/67580; 11/16/2000; Cited in IDS of 12/27/2007).

The claims are drawn to a method for identifying a compound that modulates animalia tRNA splicing endonuclease activity, the method comprising: contacting a compound or a member of a library of compounds with an animalia tRNA splicing endonuclease and a substrate for tRNA splicing endonuclease comprising a nucleic acid, wherein the nucleic acid comprises a tRNA intron within a bulge-helix-bulge structure or a mature domain of a precursor tRNA; and detecting the amount of substrate cleaved, wherein a compound that modulates animalia tRNA splicing endonuclease activity is identified if the amount of substrate cleaved in the presence of a

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compound is altered relative to the amount of substrate cleaved in the absence of the compound or in the presence of a negative control.

Tocchini-Valentini teaches methods of monitoring tRNA splicing endonuclease activity on various target molecules (see claims 1-17 and examples 1-3). Tocchini-Valentini teaches cleaving the mature domain of a tRNA molecule with the purified form (*in vitro*) and *in vivo* form animalia endonuclease (*Xenopus laevis* and murine NIH3T3 cells) (see pages 13-22 and figures 1-3). Tocchini-Valentini teaches contacting a substrate for tRNA splicing endonuclease with a tRNA splicing endonuclease (see pages 6-8 and figures 1-10). Tocchini-Valentini teaches the substrate contains bulge-helix-bulge or mature domain structure (see page 6, example 1, and figure 5). Tocchini-Valentini teaches detecting the amount of substrate cleaved (see page 7, example 2, figure 3, claims 1-17), which reads on the detecting substrate cleaved present step (b) of claim 55. The reference also teaches linking a fluorescent label with the nucleic acid substrate (e.g. GFP) (see pages 4 and 25 and figure 5). Tocchini-Valentini teaches detecting the GFP expression as an indication of the endonuclease activity (see page 25 and figure 6).

Tocchini-Valentini does not teach assaying for a compound that can reduce (or inhibit) RNA splicing.

However, Gontarek teaches methods or assays for screening for a compound that modulate splicing reactions. (see pages 11-13 and 21-26 and claims 1-16). Gontarek teaches contacting a compound to a splicing reaction to inhibit the splicing reaction (see page 2 and claim 1). The reference also teaches how the method of screening compounds can be used to identify inhibitors of splicing polypeptides compounds (see page 23).

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It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to provide Gontarek's methods of identifying a compound that modulates Tocchini-Valentini's animalia tRNA splicing endonuclease activity, comprising contacting a compound with a animalia tRNA splicing endonuclease and a substrate for tRNA splicing endonuclease, and comprising detecting the amount of substrate cleaved to arrive at applicant's invention with the above cited references before them.

A person of ordinary skill in the art would have been motivated to contact Tocchini-Valentini's animalia tRNA splicing endonuclease with compounds of interest to measure the amount of RNA splicing, because Gontarek teaches that tRNA splicing endonuclease reactions are useful for screening for compounds that inhibit the RNA splicing mechanism.

A person of ordinary skill in the art would have reasonable expectation of success to screen for compounds that modulate animalia tRNA splicing endonuclease activity because the tools to execute this method were available to the skilled artisan as evidenced by Tocchini-Valentini's and Gontarek.

Thus the present invention would have been *prima facie* obvious at the time the invention was made.

Claims 63, 69, and 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tocchini-Valentini (WO 01/92463; 12/6/2001; Cited in IDS of 01/09/2007), in combination with Gontarek (WO 00/67580; 11/16/2000; Cited in IDS of 12/27/2007) as applied to claim 55 and further in view of Marras (Nucleic Acids Research 2002 vol 30 pp 1-8).

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Tocchini-Valentini teaches methods of monitoring tRNA splicing endonuclease activity on various target molecules (see claims 1-17 and examples 1-3). Tocchini-Valentini teaches cleaving the mature domain of a tRNA molecule with the purified form (*in vitro*) and *in vivo* form animalia endonuclease (*Xenopus laevis* and murine NIH3T3 cells) (see pages 13-22 and figures 1-3). Tocchini-Valentini teaches contacting a substrate for tRNA splicing endonuclease with a tRNA splicing endonuclease (see pages 6-8 and figures 1-10). Tocchini-Valentini teaches the substrate contains bulge-helix-bulge or mature domain structure (see page 6, example 1, and figure 5). Tocchini-Valentini teaches detecting the amount of substrate cleaved (see page 7, example 2, figure 3, claims 1-17), which reads on the detecting substrate cleaved present step (b) of claim 55. The reference also teaches linking a fluorescent label with the nucleic acid substrate (e.g. GFP) (see pages 4 and 25 and figure 5). Tocchini-Valentini teaches detecting the GFP expression as an indication of the endonuclease activity (see page 25 and figure 6).

Tocchini-Valentini does not teach assaying for a compound using a nucleic acid labeled with a fluorophore and quencher.

However, Marras teaches labeling nucleic acids with a fluorophore and quencher in methods of nucleic acid detection (see entire document). Marras also teaches labeling the nucleic acid at the 5' end with a fluorophore and at the 3' end with a quencher (see page 2 and figures 1 and 2).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to label Tocchini-Valentini's nucleic acids with Marras's fluorophore and quencher to arrive at applicant's invention with the above cited references before them.

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A person of ordinary skill in the art would have been motivated to label Tocchini-Valentini's nucleic acids with Marras's fluorophore and quencher because Marras teaches nucleic acid detection using quenchers in combination with fluorophores allow for generation of a fluorescent signal from an efficient energy transfer.

A person of ordinary skill in the art would have reasonable expectation of success to detect cleaved tRNA labeled with a fluorophore and quencher because the labeling of nucleic acids was available to the skilled artisan at the time of the invention as evidenced by Marras.

Thus the present invention would have been *prima facie* obvious at the time the invention was made.

Claims 78-79, and 81-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tocchini-Valentini (WO 01/92463; 12/6/2001; Cited in IDS of 01/09/2007), in combination with Gontarek (WO 00/67580; 11/16/2000; Cited in IDS of 12/27/2007) as applied to claim 55 and further in view of Herrenknecht (Nucleic Acids Research 1988 vol 16 pp 7713-7714).

Tocchini-Valentini teaches methods of monitoring tRNA splicing endonuclease activity on various target molecules (see claims 1-17 and examples 1-3). Tocchini-Valentini teaches cleaving the mature domain of a tRNA molecule with the purified form (*in vitro*) and *in vivo* form animalia endonuclease (*Xenopus laevis* and murine NIH3T3 cells) (see pages 13-22 and figures 1-3). Tocchini-Valentini teaches contacting a substrate for tRNA splicing endonuclease with a tRNA splicing endonuclease (see pages 6-8 and figures 1-10). Tocchini-Valentini teaches the substrate contains bulge-helix-bulge or mature domain structure (see page 6, example 1, and

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figure 5). Tocchini-Valentini teaches detecting the amount of substrate cleaved (see page.7, example 2, figure 3, claims 1-17), which reads on the detecting substrate cleaved present step (b) of claim 55. The reference also teaches linking a fluorescent label with the nucleic acid substrate (e.g. GFP) (see pages 4 and 25 and figure 5). Tocchini-Valentini teaches detecting the GFP expression as an indication of the endonuclease activity (see page 25 and figure 6).

Tocchini-Valentini does not teach using human tRNA splicing endonuclease.

Herrenknecht teaches an extract containing human tRNA splicing endonuclease in the method of *in vitro* pre-tRNA splicing (see entire document).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to substitute Tocchini-Valentini's mouse tRNA splicing endonuclease with Herrenknecht's human tRNA splicing endonuclease to arrive at applicant's invention with the above cited references before them.

The present claims would have been obvious because the substitution of one known element human tRNA splicing endonuclease, taught by Herrenknecht for another mouse tRNA splicing endonuclease, taught by Tocchini-Valentini would have yielded predictable results to one of ordinary skill in the art at the time of the invention (i.e modulating human tRNA splicing endonuclease). See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

Thus the present invention would have been *prima facie* obvious at the time the invention was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

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improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 55-56, 58, 63, 65, 67, 69, 71, 73, 75, 78-79, and 81-82 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 42-64 of copending Application No. 10/551,304.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims and the claims of copending application are drawn to a method a method for identifying a compound that modulates tRNA splicing endonuclease activity comprising contacting a compound with tRNA splicing endonuclease and a substrate and detecting the amount of substrate cleaved. Therefore the present claims are obvious in view of the claims of the copending Application 10/551,304.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

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Claims 55-56, 58, 63, 65, 67, 69, 71, 73, 75, 78-79, and 81-82 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 26-48 of copending Application No. 10/551,300.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims are drawn to a method a method for identifying a compound that modulates tRNA splicing endonuclease activity comprising contacting a compound with tRNA splicing endonuclease and a substrate and detecting the amount of substrate cleaved and the claims of the copending application are drawn to method for identifying compound that modulates tRNA splicing ligase activity. The same compound can effect both tRNA splicing endonuclease and tRNA splicing ligase. Therefore the present claims are obvious in view of the claims of the copending Application 10/551,300.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTIAN BOESEN whose telephone number is 571-270-1321. The examiner can normally be reached on Monday-Friday 9:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CHRISTIAN BOESEN/

Examiner, Art Unit 4131

/James O. Wilson/

Supervisory Patent Examiner, AU 1624